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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/859,701	05/16/2001	Benjamin P. Warner	S-94,661	4132

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EXAMINER	
FOSTER, CHRISTINE E	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/859,701	WARNER ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/19/07 has been entered. Claims 1-20 are currently pending and subject to examination below.

Please note that the Examiner in this application has changed. The new Examiner, Christine Foster, may be reached at 571-272-8786.

Objections/Rejections Withdrawn

2. The rejections of claims 1-20 under § 103(a) as being unpatentable over Pirrung et al. in view of Wang is withdrawn in favor of the rejections set forth below, pursuant to further consideration by the Examiner.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant's amendments to claim 1 in the Reply of 1/19/07 insert the following limitation into step (d) of claim 1 (emphasis added):

> (d) detecting an X-ray fluorescence signal as a result of exposure to the X-ray radiation, **the X-ray fluorescence signal originating from at least any binder now bound to any member of the array**, thereby indicating that a binding event has occurred.

Applicant's Reply of 1/19/07 does not specifically indicate where the limitation that the detected X-ray fluorescence signal is one that originates solely from the binder, as now implied by the claims. The Reply discusses that the application discloses that the detected X-ray fluorescence signal can come from just the binder if the X-ray fluorescence comes from an element present in only the binder (see page 8 of the Reply of 1/19/07). This embodiment is disclosed in the specification at page 10, lines 11+.

The instant claims, in reciting methods of "detecting...the X-ray fluorescence signal originating from at least any binder now bound to any member of the array," represent broadening amendments because they are not limited to the disclosed embodiment in which the potential binder contains an element that is not present in the receptors and in which the X-ray radiation applied is of a wavelength characteristic of that element, as originally disclosed.

Although this disclosed embodiment discussed above represents a species reading on the now-claimed claimed genus, the genus is broader in scope, and would encompass other non-disclosed methods in which X-ray fluorescence originating specifically from to the binder is

selectively assessed, to the exclusion of signal due to the receptors. For example, the instant claims would encompass methods in which the presence of the binders on certain locations of the array is initially assessed by some other means, and then the X-ray fluorescence signal is measured only for those locations that are determined to have binder bound. The specification does not convey evidence of possession of such methods.

In disclosing only methods wherein X-ray fluorescence due only to the binder is detected as a result of the use of binders *that contain an element not present in the receptors*, followed by irradiation with X-rays of a wavelength characteristic of that element, the specification fails to convey evidence of possession of all methods in which the X-ray fluorescence signal originating from the binder is selectively detected.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a separation or wash step.

The disclosed methods involve detection of binding by detecting X-ray fluorescence produced by the potential binder. The presence of such fluorescence indicates that the potential binder has bound to the receptors on the array. However, the claims fail to recite any steps in which unbound potential binder would be separated from the receptors. Without such a separation step, all of the added potential binder that is exposed to the receptors would be subsequently detected, irrespective of whether it bound to receptors or not. Therefore, it is

essential to the performance of the claimed methods that unbound potential binder be separated from the sample prior to detection, e.g. through a wash step.

7. Claims 11-20 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: that the untagged binder contains an element capable of producing X-ray fluorescence.

Claim 1 recites step (d) in which an X-ray fluorescence signal is detected, "thereby indicating that a binding event has occurred". However, the claim fails to make clear that the potential binder is contributing to the X-ray fluorescence signal. If this were not the case--for example, if the receptors alone produced X-ray fluorescence--then detection of the signal would not result in detection of binding, since the signal would be produced irrespective of whether the receptors bind to the binder or not. Therefore, it is essential to the performance of the method that the potential binder be capable of producing (or at least contributing to) the X-ray fluorescence signal.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1-8, 10-18, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang (US 4,663,277) in light of Plester et al. (US 4,830,192).

Wang teach methods for detecting viruses and/or proteins, in which a plurality of viruses or proteins (i.e., receptors) in a specimen is exposed to an extended solid phase component (i.e., substrate) which is coated in at least one location with antiviral or antiprotein antibody (see especially the abstract; column 2, lines 16-67; column 3, lines 25-57; and claims 1, 20, and 39-40 in particular). This step in which viruses in the sample are bound to the solid phase via the antiviral or antiprotein antibodies reads on the claimed step of "arraying" the receptors on a substrate when given its broadest reasonable interpretation. For example, Wang teaches a solid phase that is a dipstick having two locations at which the antibody is coated (see Figure 3 and column 3, lines 65-68), such that the viruses would be bound to the dipstick in an array or pattern corresponding to the locations at which the antibody is coated. Different viruses can also be detected simultaneously by using different antiviral antibodies (column 7, lines 39-51), which would also be considered to represent an array absent a specific or limiting definition for this term.

Wang further teaches exposing the arrayed receptors to at least one potential binder, namely the same antibody coated onto a mobile solid phase of dispersed microspheres (see in particular column 2, lines 53-59; column 4, line 61 to column 5, line 2). In one embodiment, the microspheres in the binder may be doped with metal elements so as to enable detection by X-ray fluorescence using appropriate detection equipment (column 6, lines 12-20; column 7, lines 21-

59; and claims 1 and 20, for example). Detection of the X-ray fluorescence of the metal element labels in the microspheres indicates that binding between the receptors and the solid phased antibody(ies) has occurred.

It is noted that Wang teaches X-ray fluorescence detection, but does not make particular mention of whether this processed involved irradiation with X-rays to produce the fluorescence signal. Plester et al. provide evidence that X-ray fluorescence involves the excitation of sample by irradiation of the material with X-rays (column 9, lines 16-23). Therefore, in light of the evidence of Plester et al., the teachings of Wang read on the instantly claimed step of exposing the array members to X-ray radiation, since the X-ray fluorescence detection procedures of Wang would necessarily involve X-ray irradiation of the sample. That X-rays were used to produce the X-ray fluorescence signal taught by Wang would also be at once envisaged by the skilled artisan.

Although the methods of Wang involve first arraying the receptors on the extended solid phase, followed by contacting with the plurality of antibody-microsphere binders, it is noted that the instant claims do not require any particular order in which steps (a) and (b) of claims 1 and 11 are performed. Therefore, the reference reads on the claims. See MPEP 2111.01 (II).

With respect to claim 11, it is acknowledged that the claim requires the potential binder to be "untagged". However, the instant specification defines a "tagged" ligand as one that is "attached via one or more chemical bonds to a chemical portion that fluoresces when exposed to non-ionizing, ultraviolet radiation" (page 2, lines 27-30). Therefore, an "untagged" potential binder would be one that is not fluorescently tagged. See also the instant specification at page 3, lines 9-20, where "untagged" binders are discussed in terms of fluorescent tags. Since there is

nothing in this definition that would rule out attachment of moieties that fluorescence when exposed to *ionizing* radiation (i.e., X-rays), when the claims are given their broadest reasonable interpretation the antibody-microsphere binders of Wang may be considered "untagged" according to Applicant's definition since they do not contain tags that fluorescence when exposed to non-ionizing, UV radiation, but rather contain metal elements that fluorescence when exposed to ionizing X-rays (as in the instant specification).

With respect to claims 2-5 and 12-15, Wang teaches detection of proteins (e.g. viral glycoproteins), which read on the instant claims as proteins are carbon-containing polymers of amino acids (see Wang at claims 20 and 40 and column 8, lines 4-36). Similarly, the antibodies taught by Wang read on claims 6-8, 10, 16-18, and 20 since antibodies are also proteins.

10. Claims 1-5, 9-15, and 19-20 rejected under 35 U.S.C. 102(e) as being anticipated by Sano et al. (US 6,391,590 B1) in light of Plester et al. (US 4,830,192).

Sano et al. teach methods of determining metal-binding activity of streptavidin-metallothionein chimeric protein, in which the receptors (i.e., chimeric proteins) are exposed to at least one potential binder, namely the metal ion Cd^{2+} which is provided as $CdCl_2$ during the course of protein purification (Example 2, see especially column 15, lines 11-16 and 30-42; and also at column 2, lines 40-54). The reference further teaches spotting (i.e. arraying) the proteins onto a substrate (polypropylene membrane). See Example 3, in particular at column 15, lines 58-61). The arrayed proteins were then subjected to quantitative X-ray fluorescence in order to determine the amount of metals in the sample spot (Example 3).

The quantitative X-ray fluorescence procedures of Sano et al. would necessarily involve irradiation with X-rays in light of the evidence of Plester et al. that X-ray fluorescence involves the excitation of sample by irradiation of the material with X-rays (see Plester et al. at column 9, lines 16-23). Therefore, in light of the evidence of Plester et al., the teachings of Sano et al. read on the instantly claimed step of exposing the array members to X-ray radiation, since the X-ray fluorescence detection procedures disclosed by Sano et al. would necessarily involve X-ray irradiation of the sample. That X-rays were used to produce the X-ray fluorescence signal taught by would also be at once envisaged by the skilled artisan.

With respect to claims 2-5 and 12-15, the chimeric protein taught by Sano et al. reads on the instant claims as proteins are carbon-containing polymers of amino acids. Similarly, the antibodies taught by Wang read on claims 6-8, 10, 16-18, and 20 since antibodies are also proteins.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-20 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-42 of copending Application No. 10/880,388. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '388 application also recites a method in which a receptor is deposited on a substrate and exposed to a solution comprising at least one potential binder (chemical) that binds to the receptor to form a complex (see especially claim 30). Binding is detected by X-ray fluorescence; in particular, the X-ray fluorescence of the potential binder is assessed by exciting a heavy element that is present in the chemical and the receptor and subtracting a baseline X-ray fluorescence signal due to the receptor alone before binding.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 1-20 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 11/974,156. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '156 application also recites a method in which a receptor is exposed to a potential binder (chemical) that has at least one heavy element and a complex between the receptor and chemical is allowed to from (see especially claim 1). The receptor may be deposited on a substrate (see claim 2). The X-ray fluorescence signal due to the chemical is

detected by determining the net X-ray signal, from which the baseline signal due to receptor only has been subtracted, as an indication of binding affinity (claim 1).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

14. Applicant's arguments with respect to claims 1-20 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

16. Goldin et al. ("Quantitation of antibody binding to cell surface antigens by x-ray fluorescence spectrometry" Biochimica et biophysica acta, (1979 Mar 23) Vol. 552, No. 1, pp. 120-8) teaches detection of binding to cell surface antigens that have been arrayed onto electron microscope grids (i.e. substrates) by X-ray fluorescence spectrometry.

17. Wielopolski -et al. ("Determination of ruthenium on DNA by XRF" Biological Trace Element Research (1987), 13, 283-90) also teaches detection of ruthenium complexes to DNA receptors, where the sample is spotted onto foil prior to detection by XRF.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christine Foster
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01/18/08

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